

**REMARKS**

Claims 11-12, 17-25, 43-55 and 62-71 are pending. Claim 11 has been amended to delete “*Flaviviridae*” and to recite “hepatitis C.” Support for this amendment is found, for example, in original claim 12. Claim 12 has been canceled without prejudice.

Claims 11-12, 17-25, 43-55 and 62-71 stand rejected. Applicants respectfully request reconsideration of the pending rejections based on the following comments.

**Obviousness-Type Double Patenting Rejections**

**A. U.S. Patent No. 6,812,219.**

Claims 11-12, 17-25, 43-55 and 62-71 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims of U.S. Patent No. 6,812,219 (“the ’219 patent”). Specifically, the Examiner alleges that the instant claims are not distinct from the claims of the ’219 patent because “both applications are drawn to treating flavivirus infections in a host using 2’-methyl-pyrimidine nucleosides.” (Office Action, page 3). Applicants respectfully disagree.

An obviousness-type double patenting rejection is appropriate only when the claims at issue are not “patentably distinct” from the claims of a commonly owned earlier patent. *See Eli Lilly & Co. v. Barr Laboratories, Inc.*, 251 F.3d 955, 967 (Fed. Cir. 2001). A claim is not patentably distinct from an earlier patent claim if the later claim is “obvious over, or anticipated by, the earlier claim.” *Id.* at 968. Applicants request withdrawal of the double patenting rejection because the instant claims are not obvious over, or anticipated by the claims of the ’219 patent.

The instant claims recite, *inter alia*, methods of treating hepatitis C virus (“HCV”) infections using 3’-amino acid substituted 2’-methyl pyrimidine nucleosides. The ’219 patent discloses methods of treating flavivirus or pestivirus infections. HCV is not a flavivirus or a pestivirus. Indeed, the specification of the ’219 patent discloses that HCV belongs to its *own genus*, hepacivirus, which is distinct from the flavivirus and pestivirus *genuses*. (Column 12, lines 6-9). Thus, the instant claims are directed to an entirely different invention than the claims of the ’219 patent—the treatment of HCV infections, not flavivirus or pestivirus infections. The policy behind a double patenting rejection—the prevention of an unjustified extension of the term of a patent—does not support the Examiner’s rejection in this case. *See In re Kaplan*, 789 F.2d 1574, 1579 (Fed. Cir. 1986) (“the basis for...obviousness-type double

patenting rejections is timewise extension of the patent right”). Allowance of the instant claims, directed to HCV infections, would not result in the extension of the term of the ’219 patent, which covers only the treatment flavivirus and pestivirus infections. For at least these reasons, Applicants respectfully request that the double patenting rejection be withdrawn.

The Examiner cites *In re Payne* to support the general assertion that one skilled in the art would be motivated to make compounds encompassed by a genus of compounds in the prior art which have the same properties. (Office Action, page 3). Applicants point out that the recent law of obviousness in cases of alleged structural similarity requires more. Specifically, in *Takeda Chemical Ind., Ltd. v. Alphapharm Pty., Ltd.*, the court held that the compounds at issue were not *prima facie* obvious over structurally similar “compound b” because the prior art provided no motivation to modify compound b to arrive at the claimed compounds, and there was no reasonable expectation that the modification would provide the desired pharmacological properties. 429 F.3d 1350, 1360 (Fed. Cir. 2007). Indeed, the court noted that “we have cautioned ‘that generalization should be avoided insofar as specific chemical structures are alleged to be *prima facie* obvious one from the other.’” *Id.* at 1361 (quoting *In re Grabiak*, 769 F.2d 729, 731-32, (Fed. Cir. 1985)). Thus, the current law of obviousness in cases concerning structurally similar compounds “requires a showing of ‘adequate support in the prior art’ for the change in structure.” *Id.* at 1356 (quoting *Grabiak*, 769 F.2d at 729).

The Examiner asserts that “amino acid esters are known to make prodrugs.” (Office Action, page 3). Respectfully, the Examiner has provided no evidence of this assertion, nor has he provided evidence as to why one skilled in the art would be motivated to modify the compounds of the ’219 patent to arrive at the specific 3’-amino acid substituted compounds of the instant claims. Without showing support in the prior art for the change in structure, the Examiner has failed to state a *prima facie* case of obviousness. *Takeda*, 429 F.3d at 1356. Because the Examiner has failed to state a *prima facie* case of obviousness, the instant claims are patentably distinct from the claims of the ’219 patent. See *Eli Lilly*, 251 F.3d at 968.

Furthermore, even assuming, *arguendo*, that the Examiner has made a *prima facie* case of obviousness, Applicants submit that the compounds of the instant claims possess unexpected properties that rebut the *prima facie* case of obviousness. Evidence of unexpected advantageous properties of a compound may rebut a *prima facie* case of obviousness. Manual of Patent Examination Procedure (“MPEP”) § 716.02(a); *In re Chupp*, 816 F.2d. 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Applicants have discovered that

the compounds of the instant claims exhibit unexpectedly superior biological properties with respect to bioavailability and anti-viral activity. For example, treatment of HCV infected chimpanzees with a 3'-amino acid substituted 2'-methyl pyrimidine nucleoside of the instant claims resulted in significant reduction of viral loads. (Example 36 at pages 194-198 of the specification). Treatment of HCV infected human subjects with the same compound of the instant claims resulted in ready absorption and likewise gave favorable antiviral results. (Example 40 at pages 200-204 of the specification). None of these results were disclosed in the '219 patent. Thus, Applicants have presented unexpected properties that rebut the *prima facie* case of obviousness, and Applicants respectfully request that the double patenting rejection be withdrawn.

**B. U.S. Patent No. 6,914,054.**

Claims 11-12, 17-25, 43-55 and 62-71 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-27 of U.S. Patent No. 6,914,054 ("the '054 patent"). Specifically, the Examiner alleges that the instant claims are not distinct from the claims of the '054 patent because "both applications are drawn to treating flavivirus infections in a host using 2'-methyl-pyrimidine nucleoside[s]." (Office Action, page 4). Applicants respectfully disagree.

The '054 patent discloses methods of treating flavivirus or pestivirus infections, while the instant claims recite methods of treating HCV infections. As mentioned above, HCV is not a flavivirus or a pestivirus. Thus, as is the case with the '219 patent, the instant claims are directed to an entirely different invention than the claims of the '054 patent—the treatment of HCV infections, not flavivirus or pestivirus infections. Allowance of the instant claims would not result in the extension of the term of the '054 patent because the '054 covers only the treatment flavivirus and pestivirus infections. Therefore, Applicants respectfully request that the double patenting rejection be withdrawn.

Moreover, the instant claims are not obvious over the claims of the '054 patent because the Examiner has not shown adequate support for the change in structure from the unsubstituted nucleosides of the '054 patent to the specific 3'-amino acid ester substitution of the instant claims. Because the Examiner has not put forth any evidence from the prior art as to why one skilled in the art would be motivated to modify the compounds of the claims of the '054 patent to arrive at the compounds of the instant claims, a *prima facie* case of obvious cannot be made. *Takeda*, 429 F.3d at 1356. Further, the unexpected properties discussed above with respect to the '219 patent were not disclosed in the '054 patent. Thus, Applicants

have presented unexpected properties that rebut the *prima facie* case of obviousness. Therefore, because the claims of the '054 patent do not teach or suggest the compounds of the instant claims, and Applicants have presented unexpected properties to rebut any *prima facie* case of obviousness, the methods of the instant claims are not obvious, and therefore patentably distinct from the claims of the '054 patent.

**C. U.S. Patent No. 7,105,493.**

Claims 11-12, 17-25, 43-55 and 62-71 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-2 and 8-18 of U.S. Patent No. 7,105,493 ("the '493 patent"). Specifically, the Examiner alleges that it would be "obvious to practice the invention of the '493 patent on another member of the Flaviviridae virus family, HCV." (Office Action, page 2). Applicants respectfully disagree.

The '493 patent discloses methods of treating flavivirus or pestivirus infections, while the instant claims recite methods of treating HCV infections. As mentioned above, HCV is not a flavivirus or a pestivirus. Thus, as is the case with the '493 patent, the instant claims are directed to an entirely different invention than the claims of the '493 patent—the treatment of HCV infections, not flavivirus or pestivirus infections. Allowance of the instant claims would not result in the extension of the term of the '493 patent because the '493 covers only the treatment flavivirus and pestivirus infections. Therefore, Applicants respectfully request that the double patenting rejection be withdrawn.

Moreover, the instant claims are not obvious over the claims of the '493 patent because the Examiner has not shown adequate support for the change in structure from the unsubstituted nucleosides of the '493 patent to the specific 3'-amino acid ester substitution of the instant claims. Because the Examiner has not put forth any evidence from the prior art as to why one skilled in the art would be motivated to modify the compounds of the claims of the '493 patent to arrive at the compounds of the instant claims, a *prima facie* case of obviousness cannot be made. *Takeda*, 429 F.3d at 1356. Again, the unexpected properties discussed above with respect to the '219 and '054 patents were not disclosed in the '493 patent. Thus, Applicants have presented unexpected properties that rebut the *prima facie* case of obviousness. Therefore, because the claims of the '493 patent do not teach or suggest the compounds of the instant claims, and Applicants have presented unexpected properties to rebut any *prima facie* case of obviousness, the methods of the instant claims are not obvious, and therefore patentably distinct from the claims of the '493 patent.

**D. U.S. Patent Application No. 10/602,691.**

The Examiner has provisionally rejected claims 11-12, 17-25, 43-55 and 62-71 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims of co-pending U.S. Patent Application No. 10/602,691 ("the '691 application"). Applicants respectfully disagree.

The compounds of the instant claims are patentably distinct from those of the '691 application. The instant claims recite 3'-*amino acid substituted* 2'-methyl pyrimidine nucleosides. The claims of the '691 application do not recite 3-amino acid substitution. Furthermore, the claims of the '691 application provide no motivation to one skilled in the art to modify the compounds claimed therein to include 3'-amino acid substitution, nor does the Examiner point to where such alleged motivation exists. Without articulating a reason why one skilled in the art would be motivated to modify the compounds of the '691 application to arrive at the compounds of the instant claims, the Examiner has failed to state a *prima facie* case of obviousness. *See Takeda*, 429 F.3d at 1356 (obviousness in cases concerning structurally similar compounds requires a showing of support in the prior art for the change in structure). Thus, because the instant claims do not overlap with and are not obvious over the claims of the '691 application, the instant claims are patentably distinct from the claims of the '691 application. *See Eli Lilly*, 251 F.3d at 967. For at least these reasons, Applicants respectfully request that the double patenting rejection be withdrawn.

**E. U.S. Patent Application Nos. 11/005,440; 11/005,443 and 11/005,446.**

The Examiner has provisionally rejected claims 11-12, 17-25, 43-55 and 62-71 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over the claims of co-pending U.S. Patent Application Nos. 11/005,440; 11/005,443 and 11/005,449. Applicants respectfully point out that Serial No. 11/005,449 does not share a common inventor or common ownership with respect to the instant application. Applicants believe the Examiner intended to cite Serial No. 11/005,446, which does share common inventors and is commonly owned with respect to the instant application.

Because Serial Nos. 11/005,440; 11/005,443 and 11/005,446 are pending applications, Applicants request abeyance of this issue until an indication of allowable subject matter in each application. If provisional obviousness-type double patenting rejections are the only rejections remaining in an earlier filed pending application, the Examiner should withdraw

those rejections and permit the earlier-filed application to issue as a patent without a Terminal Disclaimer. MPEP § 804, subsection I.B.

The filing date of the instant application is June 27, 2003. Serial Nos. 11/005,440; 11/005,443 and 11/005,446 were each filed on December 6, 2004. Therefore, because the instant application is the earlier-filed application, and only provisional obviousness-type double patenting rejections remain, Applicants respectfully request that the Examiner withdraw the rejection and allow the instant application to issue as a patent without a Terminal Disclaimer.

**CONCLUSION**


In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

Please apply fees for a extension of time for three months (\$1,050.00), and any other charges, or any credits, to Jones Day Deposit Account No. 503013 (ref. no. 417451-999016).

If the Examiner believes it would be useful to advance prosecution, the Examiner is invited to telephone the undersigned at (858) 314-1200.

Respectfully submitted,

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